UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,720	03/03/2004	Shinn-Chih Wu	WUSH3012/EM	2654

23364 7590 11/07/2005

BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/790,720	WU ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 8-26-05 has been entered. Claims 28, 29 and 32 have been amended. Claims 36-43 have been added. Claims 28-43 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 8-26-05 necessitates this new ground of rejection.

Claims 36-43 are newly added claims and are very similar to claims 28-35. One difference between claims 28-35 and the newly added claims 36-43 is that claim 28 refers to "expression genetic insert" and claim 36 refers to "expression plasmid". Another difference is that claim 36 recites "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo".

The phrase "wherein said mammary gland specific promoter is bovine alpha-lactalbumin promoter" in claim 40 is vague and renders the claim indefinite. There are three phrases of "a mammary gland specific promoter" in claim 36. It is unclear which "mammary gland specific promoter" is referred to in claim 40.

3. Claim 36 recites the limitation "**the** DNA sequences" in line 4. There is insufficient antecedent basis for this limitation in the claim. Claims 37-43 depend from claim 36 but fail to

clarify the indefiniteness. Applicants' amendment filed 8-26-05 necessitates this new ground of rejection.

4. Claims 36-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 8-26-05 necessitates this new ground of rejection.

The phrase "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo" in claim 36 step (b) is vague and renders the claim indefinite. It was well known in the art the transgene is injected into a pronucleus of a fertilized egg and said egg is transferred to the oviduct of a pseudopregnant foster mother for the development of embryo and transgenic animal (no porcine embryonic stem cells has been successfully used for germ line transmission of transgene via homologous recombination method). It appears that the gene is injected into a pronucleus of a fertilized egg or an embryo and then implanted into a non-human animal. The term "embryonic implantation" seems to mean that an embryo is implanted into something. It is unclear how to transfer an expression plasmid by embryonic implantation into a **swine embryo**.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 28-35 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and is repeated for the reasons set forth in the preceding Official action mailed 4-26-05. Applicant's arguments filed 8-26-05 have been fully considered but they are not persuasive.

Applicants argue that the written description requirement does not require exact language set forth in the claim be recited in the specification and one of ordinary skill would understand the expression "genetic insert" as inclusive of the plasm(a)id described in the present invention. Similarly, the phrase "synchronized recipient" would be understood by one ordinary skill because synchronization is necessary for the transference (amendment, p. 9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-26-05. The term "genetic insert" is broader than the term "plasmid". Plasmid is a well-known vector in the art that it contains origin of replication, multiple cloning sites, promoter for expression and selectable markers etc., for gene expression in bacteria. However, the term "genetic insert" is a much broader term that it encompasses any DNA sequence that can be inserted into another DNA sequence. The specification fails to provide sufficient description for the phrase "expression genetic insert". On the other hand, although synchronization was known to be necessary for the transference, however, the specification must provide sufficient description for transplanting an embryo into a synchronized recipient but fails to do so. Thus, the phrase "expression genetic insert" in claim 28 and the phrase "transplanting said embryo ... into a **synchronized recipient**" in step (c) of claim 28 are still considered new matter.

7. Claims 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' amendment filed 8-26-05 necessitates this new ground of rejection.

Claims 36-43 are newly added claims and are very similar to claims 28-35. One difference between claims 28-35 and the newly added claims 36-43 is that claim 28 refers to "expression genetic insert" and claim 36 refers to "expression plasmid". Another difference is that claim 36 recites "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo".

The phrase "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo" is considered new matter. The specification describes "transferring said expression plasmid ... by means of gene injection **and** embryonic implantation **to a non-human mammal**" (specification, p. 5, lines 9-11). The phrase "gene injection and embryonic implantation to a non-human mammal" is different from "gene injection or embryonic implantation into a swine embryo". As discussed above under 35 U.S.C. 112 second paragraph rejection, it is unclear how to transfer an expression plasmid by embryonic implantation into a **swine embryo**. The specification fails to provide sufficient description for "transferring said expression plasmid by gene injection **or** embryonic implantation **into a swine embryo**". Thus, the phrase "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo" is considered new matter.

8. Claims 28-30 and 32-35 remain rejected and the newly added claims 36-38 and 40-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a 1:1 mixture of plasmids, one comprising a mammary gland specific promoter operably linked to a trasngene encoding human clotting factor IX (hFIX) and the other comprising a mammary specific promoter operably linked to a transgene encoding porcine lactoferrin, to produce a transgenic swine whose somatic and germ cells comprise said transgenes via introducing said trasngenes into a swine embryo, does not reasonably provide enablement for a method for producing a trasngenic swine whose somatic and germ cells comprise said transgenes by using a mixture of the plasmids set forth above other than the 1:1 ratio of said plasmids via introducing said trasngenes into a swine embryo so as to produce and secrete hFIX and porcine lactoferrin in the mammary tissue of said swine and to isolate these proteins from the milk of said swine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 4-26-05. Applicant's arguments filed 8-26-05 have been fully considered but they are not persuasive.

Claims 36-43 are newly added claims and are very similar to claims 28-35. One difference between claims 28-35 and the newly added claims 36-43 is that claim 28 refers to "expression genetic insert" and claim 36 refers to "expression plasmid". Another difference is that claim 36 recites "transferring said expression plasmid by gene injection or embryonic implantation into a swine embryo".

Applicants argue that a patent needs not teach what is well known in the art, the 1:1 ratio of the expression transgene plasmid is the best ratio to produce the transgenic swine and one skilled in the art would appreciate that other ratios may be used. Applicants cite Figure 4 and example 5 and argue that one can improve gene expression efficiency by applying pre-mRNA processing, post-mRNA processing or other modification technology and the method disclosed in the present invention shows transfer of two or more genes into swine and stably expression of said gene throughout the lactating period of the swine, and the transgene passes into the offsprings of transgenic swine (amendment, p. 7-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-26-05. Application of pre-mRNA processing, post-mRNA processing or other modification technology may be able to improve gene expression efficiency, however, as discussed in the preceding Official action mailed 4-26-05, the art of making transgenic animal in general was unpredictable at the time of the invention. Individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct, and the site of integration, etc., are the important factors that governs the expression of a transgene. Variation in the genetic background also contributes to unpredictable resulting phenotypes of transgenic or gene-targeted animals. There are genetic background variations among different pigs and many of the phenotypes of transgenic porcine are influenced by the genetic backgrounds of the pigs. Further, the art of recombinant protein production in the milk of transgenic animal was unpredictable at the time of the invention. It is difficult to predict that a construct will be functional because of insufficient knowledge on gene transcript, Pre-MRNA processing, RNA and protein stability. Integration of the microinjected transgene is aleatory resulting in highly variable levels of expression, and possible detrimental effects. The

claims encompass numerous different ratios of the two different expression transgenes used to generate transgenic swine. While 1:1 ratio of transgenes encoding hFIX and porcine lactoferrin can generate transgenic porcine having germ line transmission of said transgenes, however, how and whether the hFIX and porcine lactoferrin proteins are going to be expressed under numerous different ratios of expression transgenes expressing these two proteins is unclear and the resulting phenotype of the transgenic swine produced would be unpredictable. Therefore, one skilled in the art at the time of the invention would require specific guidance and undue experimentation to practice over the full scope of the invention claimed.

Conclusion

No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER